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Acute Idiosyncratic Reaction to Hydrochlorothiazide Ingestion

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ADMINISTRATION OF THIAZIDE DIURETICS has been reported to produce various idiosyncratic reactions including skin rash,¹ urticaria, photosensitivity,² jaundice, necrotizing vasculitis³ and bone marrow depression.⁴⁻⁷

There have been six reported cases of idiosyncratic pulmonary edema reactions immediately following the ingestion of hydrochlorothiazide.⁸⁻¹² These previously reported cases have not been associated with bone marrow depression. We report a case of hydrochlorothiazide-induced acute pulmonary edema and associated severe leukopenia and thrombocytopenia in a patient shortly after she ingested a single 50-mg tablet of hydrochlorothiazide.

Report of a Case

A 50-year-old woman entered the Los Angeles County-University of Southern California Medical Center emergency room in April 1980 because of nausea, vomiting and light-headedness. She had been in her usual state of good health aside from a history of mild hypertension, untreated except for salt restriction. The day of admission she had seen a physician and was given hydrochlorothiazide for mild hypertension. Two and a half hours after taking the first 50-mg tablet, nausea and vomiting developed and she became light-headed. She took no other medication.

She stated that a similar problem had occurred two years previously after taking hydrochlorothiazide and she had not taken the drug again. She said she had had no previous cardiac or pulmonary disease. She did not smoke.

On physical examination she was noted to be slightly obese and appeared mildly distressed. Her skin was diaphoretic and cool. Blood pressure was 90/60 mm of mercury without postural changes, pulse rate was 110 beats per minute and regular, respirations were 18 per minute and the temperature (taken orally) was 35.8°C. There was no neck vein distension. Auscultation of the chest showed decreased breath sounds at

both lung bases. On examination of the heart she had neither murmurs nor gallops. There was no calf tenderness, clubbing or edema. The remainder of the examination showed no abnormalities.

Admission laboratory data within normal limits included serum enzymes, bilirubin, calcium, phosphorous, blood urea nitrogen, creatinine, serum albumin, total protein and serum electrolytes. Analysis of urine gave normal findings. The initial leukocyte count was 1,200 per cu mm, with 40 percent segmented neutrophils, 58 percent lymphocytes and 2 percent monocytes. No eosinophils or band forms were seen. The antinuclear antibody titer was positive at 1:20. The hemoglobin level was 15.4 grams per dl, hematocrit 45.2 percent and the platelet level appeared to be decreased. The electrocardiogram appeared unremarkable, but the chest x-ray study showed pulmonary edema (Figure 1) when compared with a normal film taken two months earlier (Figure 2).

The arterial blood gas determinations made 24 hours after admission while the patient was breathing room air showed an oxygen partial pressure of 74 mm of mercury, a carbon dioxide partial pressure of 30 mm of mercury and a pH of 7.47. The platelet count was 86,000 per cu mm. Various viral titers were negative, including cold agglutinins and complement fixation for histoplasmosis and coccidioidomycosis.

On admission to hospital, initial treatment included administration of oxygen and intravenous replacement of fluids. The patient responded well and had no further respiratory distress; no systemic corticosteroids or other medicines were given. The leukocyte count rose to 6,700 per cu mm after four days, with a normal differential count, and the platelet count returned to within normal limits. She was discharged after four days in hospital; no abnormalities were noted on an x-ray film of the chest.

Discussion

In view of the present widespread use of thiazide diuretics, the life-threatening adverse effects of these compounds are of great practical import. The spectrum of other significant drug-induced pulmonary disease has been reviewed in the past.¹³ The previous reports of thiazide-induced pulmonary edema were not associated with severe bone marrow depression, though bone marrow depression due to the ingestion of hydrochlorothiazide has been reported,^{4,7} and at least one case of hydrochlorothiazide-induced pulmonary edema was associated with moderate leukopenia.¹² Thiazide diuretics are frequently prescribed for edematous states and often for congestive heart failure. In our patient there had been no previous history of organic heart or pulmonary disease; as a matter of fact, the patient had had normal findings, except for transient hypertension, at a clinical examination two months earlier.

Apparently a similar reaction had occurred earlier in this patient after ingestion of a single thiazide tablet. The sequence of events following the last oral ingestion of a single thiazide tablet suggests an idiosyncratic re-

Refer to: Prupas HM, Brown D: Acute idiosyncratic reaction to hydrochlorothiazide ingestion. *West J Med* 1983 Jan; 138:101-102.

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Submitted, revised, December 1, 1981.

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action to thiazide, though the earlier history suggests prior sensitization is possible. If the pathogenesis had been on the basis of an allergic reaction, the patient may have benefited from corticosteroid therapy, but this was not instituted.

Although in this case and previous reports hydrochlorothiazide definitely appears to be causal, in only one instance was the patient again given the drug and the causal effect verified.¹⁰ It seems unwarranted in

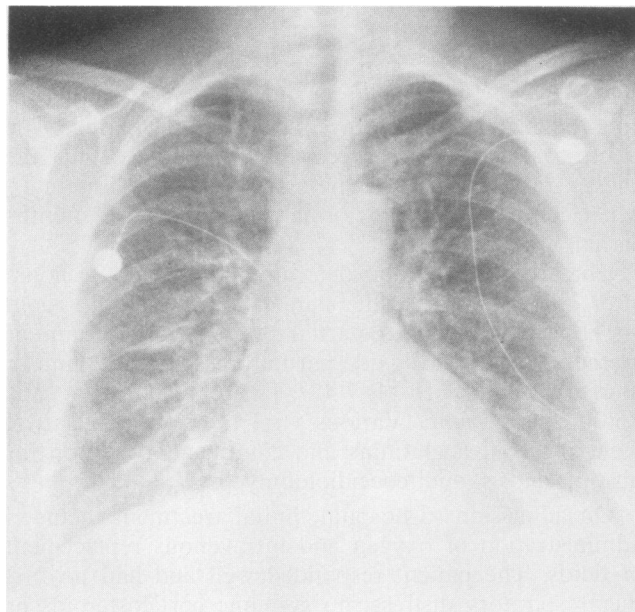


Figure 1.—Chest x-ray film taken on admission showing bilateral interstitial pulmonary edema with a normal heart size.

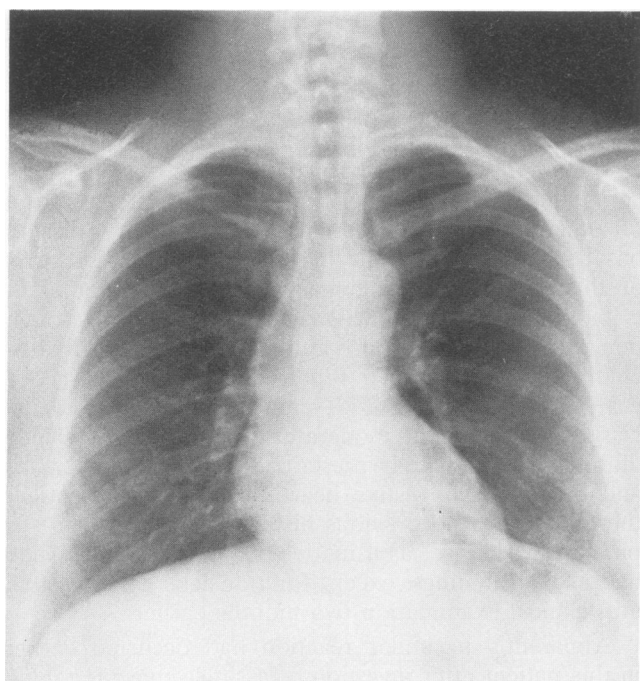


Figure 2.—Chest x-ray film taken two months before admission showing clear lung fields and a normal heart size.

our case to risk a second untoward reaction to prove the association was causal. The temporal relationship of the idiosyncratic reaction and the oral ingestion of a single tablet incriminates the diuretic.

From other published reports it is clear that a small number of patients have been recognized to have severe untoward reactions to taking thiazide diuretics, and presumably there are some patients who have a similar sequence of events but who go unrecognized. Even so, this is a most unusual response to such a commonly prescribed drug. It should alert physicians to serious reactions from the ingestion of a commonly prescribed drug.

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Mycobacterium xenopi Pulmonary Disease

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Mycobacterium xenopi is a nontuberculous mycobacterium that has been classified as a Runyon group III organism in the past along with the related *Mycobacterium avium-intracellulare* complex, with which it is sometimes confused.¹ It is a scotochromogenic organism that can cause in humans clinical infection resembling pulmonary tuberculosis. Recognized infection with this organism is uncommon, with only five reported cases in the United States.²⁻⁵ Unlike organisms isolated from

Refer to: Platia EV, Vosti KL: *Mycobacterium xenopi* pulmonary disease. *West J Med* 1983 Jan; 138:102-105.

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Submitted July 24, 1981.

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